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Danielle Gamache /Danielle Gamache/ Date: May 3, 2012

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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

**Johannes Bartholomaus**

Serial No.: 10/596,194

Filed: June 2, 2006

I.A. Filed: December 13, 2004

Art Unit: 1617

Examiner: Yu, Gina C.

Confirmation No.: 3326

Customer No.: 20999

Atty. Docket No.: 512100-2057

**ADMINISTRATION FORM BASED ON CROSS-LINKED HYDROPHILIC POLYMERS**

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

## REPLY BRIEF

SIR:

In response to the Examiner's Answer mailed march 5, 2012, and further to Applicant's Brief on Appeal filed on December 28, 2011, please reconsider the appeal in the above referenced application in light of the following comments.

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## I. STATUS OF ALL CLAIMS

Claims 1-6, 15 and 18-22 are under examination and were finally rejected in the Office Action mailed on 29 April 2011.

## II. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. Whether Claim 15 is indefinite under 35 U.S.C. § 112, second paragraph.

2. Claims 1, 6-15 and 18-22 are unpatentable under 35 U.S.C. § 103(a) being obvious over U.S. Patent No. 6,780,504 to Rupprecht et al. ("Rupprecht") in view of U.S. Patent No. 6,153,222 to Becher ("Becher") and U.S. Patent No. 6,177,096 to Zerbe et al. ("Zerbe").

3. Whether Claims 1, 6-15 and 18-22 are unpatentable under 35 U.S.C. § 103(a) being obvious over Rupprecht in view of Becher and U.S. Patent 6,177,096 to Lydzinski et al. ("Lydzinski").

## III. ARGUMENT

### A. SUMMARY OF RELEVANT LAW

The determination of obviousness rests on whether the claimed invention as a whole would have been obvious to a person of ordinary skill in the art at the time the invention was made. In determining obviousness, four factors should be weighed: (1) the scope and content of the prior art, (2) the differences between the art and the claims at issue, (3) the level of ordinary skill in the art, and (4) whatever objective evidence may be present. Obviousness may not be established using hindsight or in view of the teachings or suggestions of the inventor. The Examiner carries the burden under 35 U.S.C. § 103 to establish a prima facie case of obviousness and must show that the combination of the references relied on teach or suggest all of the limitations of the claims.

To establish a prima facie case of obviousness, the Examiner must also identify an explicit reason that would have prompted a person of ordinary skill in the art to combine the teachings of the cited references. *K.S.R. Int'l Co. v. Teleflex, Inc.*, 127 S.Ct. 1727, 1741 (2007) (citing *In re Kahn*, 441 F.3d 977, 988 (CA Fed. 2006) ("The Examiner must determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. To facilitate review, *this analysis should be made explicit*.") The Supreme Court has emphasized that "[r]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *Id.* (emphasis added).

In order to establish a *prima facie* holding of obviousness, all elements of the claims must be taught, there must be a suggestion or motivation to modify the references either from the references themselves or from knowledge available to those of skill in the art and there must a reasonable expectation of success for the modification. However, none of these requirements for establishing obviousness has been met.

Once the applicant has presented rebuttal evidence, Office personnel should reconsider any initial obviousness determination in view of the entire record. See e.g., *In re Piasecki*, 745 F.2d 1468, 1472, 223 USPQ 785, 788 (Fed. Cir. 1984).[1]

When prima facie obviousness is established and evidence is submitted in rebuttal, the decision-maker ***must start over. . . . An earlier decision should not***, as it was here, be considered as set in concrete, and applicant's rebuttal evidence then ***be evaluated only on its knockdown ability.*** Analytical fixation on an earlier decision can tend to provide that decision with an undeservedly broadened umbrella effect. Prima facie obviousness is a legal conclusion, not a fact. Facts established by rebuttal evidence must be evaluated along with the facts on which the earlier conclusion was reached, ***not against the conclusion itself.*** . . . [A] final finding of obviousness may of course be reached, but such finding will rest upon evaluation of all facts in evidence, uninfluenced by any earlier conclusion reached by an earlier board upon a different record." *In re Rinehart*, 531 F.2d 1048, 1052, 189 USPQ 143, 147 (CCPA 1976)(emphasis added).

## B. CLAIM 15 IS NOT INDEFINITE UNDER 35 U.S.C. § 112, SECOND PARAGRAPH.

On page 2 of the current Office Action, and page 4 of the Examiner's Answer, Examiner rejects Claim 15 under 35 U.S.C. § 112, second paragraph, as being indefinite. This rejection is respectfully traversed and believed overcome in view of the following discussion.

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[1] (Citation from *In re Piasecki*) "If rebuttal evidence of adequate weight is produced, ***the holding of prima facie obviousness, being but a legal inference from previously uncontradicted evidence, is dissipated***. Regardless of whether the *prima facie* case could have been characterized as strong or weak, ***the examiner must consider all of the evidence anew.*** The process is as stated in *In re Rinehart, 531 F.2d 1048, 1052, 189 U.S.P.Q. 143, 147 (CCPA 1976)*:

> When prima facie obviousness is established and evidence is submitted in rebuttal, the decision-maker must start over. . . . An earlier decision should not, as it was here, be considered as set in concrete, and applicant's rebuttal evidence then be evaluated only on its knockdown ability. Analytical fixation on an earlier decision can tend to provide that decision with an undeservedly broadened umbrella effect. Prima facie obviousness is a legal conclusion, not a fact. Facts established by rebuttal evidence must be evaluated along with the facts on which the earlier conclusion was reached, not against the conclusion itself. . . . [A] final finding of obviousness may of course be reached, but such finding [*14] will rest upon evaluation of all facts in evidence, uninfluenced by any earlier [*1473] conclusion reached by an earlier board upon a different record." (emphasis added)

*1. Previous Arguments*

Claim 15 is not indefinite as one of ordinary skill in the art would understand the scope and meaning buccal administration.

Claim 1 which encompassed the scope of administration being either transmucosal or transdermal. Claim 15 is dependent upon claim 1 and one of ordinary skill in the art would understand that the scope of administration has been limited to buccal administration. (If it would serve to expedite matters, the applicants authorize an Examiner's amendment to delete the phrase "or transdermal" if this is the only matter precluding allowability).

*2. Reply to Examiner's Answer*

Examiner responds by asserting that the above statement is an admission that Claim 15 is ambiguous. This is patently incorrect. Rather the above statement makes it clear that one of ordinary skill in the art would not be confused as to the meaning of Claim 15. Put another way, Claim 15 clearly states that "the transmucosal or transdermal administration" is "buccal administration". In other words, grammatically, it is clear that the recitation of "buccal administration" relates to the phrase "the transmucosal or transdermal administration" as a whole, rather than to each portion of the phase individually as Examiner asserts. This is the same as saying that "the transmucosal or transdermal administration" is "transmucosal administration" which is "buccal administration", only is less wordy and confusing, and thus actually more clear.

In fact, Examiner's own assertions contradict the indefiniteness rejection, and actually support Applicant's arguments. In particular, Examiner **admits** that buccal administration is inherently transmucosal and cannot be transdermal. As such, one of ordinary skill in the art would clearly know that stating that "the transmucosal or transdermal administration" is "buccal administration" restricts the "the transmucosal or transdermal administration" to a buccal, inherently transmucosal, administration.

*3. Conclusion*

Accordingly, Applicant respectfully asserts that Claim 15 is definite. Therefore, Applicant respectfully requests that the Board reverse the rejection of Claim 15 under 35 U.S.C. § 112, second paragraph.

C. CLAIMS 1, 6-15, AND 18-22 ARE NOT UNPATENTABLE UNDER 35 U.S.C. § 103(A) AS BEING OBVIOUS OVER U.S. PATENT NO. 6,780,504 TO RUPPRECHT ET AL. ("RUPPRECHT") IN VIEW OF U.S. PATENT NO. 6,153,222 TO BECHER ("BECHER") AND U.S. PATENT NO. 6,177,096 TO ZERBE ET AL. ("ZERBE").

On page 3 of the current Office Action, and page 5 of the Examiner's Answer, Examiner rejects Claims 1, 6-15, and 18-22 under 35 U.S.C. § 103(a) as being unpatentable over Rupprecht in view of Becher and Zerbe. These rejections are respectfully traversed and believed overcome in view of the following discussion.

*1. Previous Arguments*

(a) **Background**

As might be surmised from the appellation of Chien I and Chien II, both of these references, while not claiming priority over each other, do have certain similarities as befitting references with two common inventors, a common assignee and being directed toward transdermal delivery of an active substance.

As noted in the appellants' earlier response, plasticizers represent an organic compound added to a high polymer both to facilitate processing and to increase the flexibility and toughness of the final product by internal modification (solvation) of the polymer molecule. (see footnote 1 from page 7 of appellants 9 February 2011 response).

The appellants' specification discloses that for better handling of relatively brittle polymer films, i.e. in particular to increase the elasticity, softness and flexibility, plasticizers are employed in an amount of up to 20% by weight based on the amount of polymer.

When the percentage amounts of plasticizer are relatively high, phase separations may occur, e.g. due to crystallization, so that the films are no longer transparent and their physical properties such as the tear strength are adversely affected. For example, addition of 30% by weight of triethyl citrate, based on the total amount of a crosslinked hydrophilic polymer, leads to white films. The plasticizer may in fact separate out of the film. (See page 2, lines 23-37 of the appellants' specification).

**(b) Combination of Rupprecht, Becher and Zerbe Does Not Teach the Use of 30% to 60% By Weight of Glycerol As a Plasticizer In the Appellants' Dosage Form**

Rupprecht refers to a multi-layer film which includes an active substance containing layer which may be produced from a suitable film-forming, water soluble polymer (including hydroxypropylmethylcellulose) and a crosslinking agent (including tannins). See col. 3, lines 1-3 and lines 15-17.

However, the final rejection acknowledges that both Rupprecht and Becher do not teach adding glycerol in an amount of 30% to 60% by weight (see page 4, lines 13-14 and lines 21-22).

The entire specification of Rupprecht does not mention the use of a plasticizer or glycerol as part of their multi-layer film.

Becher does mention the use of a softener which includes polyethylene glycol and glycerol, but not the specific amount and not in the context of a film such as Rupprecht's. Becher refers to a volume-expandable, sheet-like application form which has a highly absorbent hydrogel former which swells on contact with water and assumes several times its original volume (see Abstract of Becher).

Unsurprisingly, because Becher is referring to a highly absorbent hydrogel former, Becher does not use a hydroxypropylmethylcellulose crosslinked with tannins and/or partially neutralized polyacrylic acid.

Becher refers to the use of crosslinked polymers like carboxyvinyl copolymers (e.g. AquaKeep®) and/or crosslinked polyvinyl pyrrolidone (e.g. Kollidone® 90) as film formers in combination with glycerol as softener carboxyvinyl copolymers is a super absorbent polymer based on polyacrylate. Polyvinylpyrrolidone (PVP) is a water-soluble polymer made from the monomer N-vinylpyrrolidone (col. 2, lines 34-39, 56-63).

Zerbe is relied upon for a teaching for the specific amount of glycerol especially with respect to Example 1 (6 g of glycerol and 30 g of hydroxypropylmethyl cellulose was used - 20% by weight which is still outside the appellants' claimed range of 30% to 60% by weight).

However, Zerbe refers to film forming ***non-crosslinked*** polymers comprising preferred water-soluble polymers selected from water-soluble cellulose derivates and polyacrylates, among others and one or more plasticizers or surfactants and one or more

polyalcohols (col. 2, line 32-36). Glycerol is mentioned as an example of a polyalcohol (col. 3, line 10-15). The references teach 20% of glycerol based on the total amount of the hydrophilic polymer, but not of the crosslinked hydrophilic polymer.

For these reasons alone, the combination of Rupprecht, Becher and Zerbe does not teach the appellants' dosage form comprising at least one active ingredient-containing and/or nutrient-containing layer based on in-situ crosslinked hydroxypropylmethylcellulose which comprises from 30% to 60% by weight of glycerol as plasticizer, based on the total amount of crosslinked hydrophilic polymers and whereby the hydroxypropylmethylcellulose has been crosslinked with tannin and/or a crosslinked, optionally partially neutralized polyacrylic acid.

### (c) The Facts of *In re Aller* Are Not Analogous to the Present Application

MPEP 2144.04 states that "...if the facts in a prior legal decision are sufficiently similar to those in an application under examination, the examiner may use the rationale used by the court."

The final rejection relies notes the holding of *In re Aller* whereby when the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation, presumably to account for the fact that the combination of Rupprecht, Becher and Zerbe did not teach the "30% to 60% by weight of glycerol" limitation. The *Aller* decision is also cited in MPEP 2144.05, section II.A.

However, the very next section in the MPEP, i.e. MPEP 2144.05, section II.B, states that "[a] particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977)."

When facts of the presently claimed invention and prior art relied upon are considered, there is no inference from any of Rupprecht, Becher or Zerbe that optimizing the amount of glycerol would have constituted a results effect variable within the context of their respective inventions and certainly does not suggest a correlation between the amount of glycerol and cross-linked hydroxypropylmethylcellulose as is claimed by the appellants.

Furthermore, as noted in the appellants' description of the state of the art, the amount of plasticizer was not thought of as being a results effective variable, i.e. amounts of plasticizer over 20% by weight were thought to produce deleterious effects. It was surprising that the selection of a specific type of crosslinked hydrophilic polymers (hydroxypropylmethylcellulose) and specific type of plasticizer (glycerol) would allow for greater content of glycerol than thought possible by those of skill in the art prior to the appellant's claimed invention.

**(d) Appellants Disclosed Evidence of Unexpected Results**

As noted in the appellants' description of the state of the art, other types of plasticizers, e.g. triethyl citrate, did not result in the desired effects for a dosage form.

The appellants also tested against other plasticizers, including those cited in Becher and Zerbe (i.e. polyethylene glycol) and showed evidence of unexpected results.

Figures 1 and 3 in the appellants' specification showed that the use of glycerol in amounts greater than 20% by weight resulted in more desirable products that when polyethylene glycol, sorbitol or triethylcitrate were used as plasticizers and that even when comparing glycerol against itself (20% by weight vs. 50% by weight) a more favorable product was obtained at the higher levels of glycerol content (see Figure 2).

***2. Reply to Examiner's Answer***

The Examiner's Answer dated March 5, 2012, still seems to overlook, and fails to adequately address, the many of the appellants' arguments above. Further, the Examiner's arguments presented in the Examiner's Answer fail to address the deficiencies of the current rejection.

More specifically, Examiner cites to Rupprecht as relating to a crosslinked hydrophilic polymer and teaching all the requirements of Claim 1 except for the inclusion of glycerol as a plasticizer. As such, Examiner cites to Becher as teaching using a softener (which can be glycerol) with a crosslinked polymer, and cites to Zerbe as teaching how much plasticizer to use in a water soluble film (which is not disclosed as contain any crosslinked polymers).

Examiner then asserts that it would be obvious to incorporate the glycol as softener of Becher (used with a crosslinked polymer not disclosed as being hydrophilic) in the

amount of glycol taught by Zerbe (which dos not relate to the use of any crosslinked polymers), into the product of Rupprecht (which specifically relates to crosslinked hydrophilic polymers). However, Examiner has established no reasonable expectation of success of such a combination, especially in view of Applicant's prior arguments above.

In particular, Rupprecht actually doesn't teach using any plasticizer at all with a crosslinked **hydrophilic** polymer. As such, the entire combination of Becher (teaching the use of a softener with a crosslinked polymer) with Rupprecht hinges on the assertion that there is a reasonable expectation of success of combining a softener (assumably as a plasticizer) as taught by Becher into the product of Rupprecht.

However, as Applicant has clearly explained above, plasticizers **in general** are not necessarily suitable in the film of Claim 1 (and thus also the combination asserted by Examiner). In particular, Applicant has explained how the use of glycerol in amounts greater than 20% by weight resulted in more desirable products that when polyethylene glycol, sorbitol or triethylcitrate were used as plasticizers and that even when comparing glycerol against itself (20% by weight vs. 50% by weight) a more favorable product was obtained at the higher levels of glycerol content (see Figure 2). As such, success of using plasticizers in general with a crosslinked hydrophilic polymer would **not** be reasonably expected by one of ordinary skill in the art. As such, there can be **no** reasonable expectation of success of including the softener of Becher in the crosslinked hydrophilic polymer product of Rupprecht (which is the only way Examiner arrives at combining glycerol with a crosslinked hydrophilic polymer). For this reason alone, Examiner's asserted combination must fail as providing a case of obviousness.

In addition, Examiner points to Zerbe as teaching ho much glycerol to use. However, the glycerol in Zerbe is used as a polyalcohol and not as a plasticizer, which are described separately from each other. Zerbe, Col. 2, Lns. 31-36; and Claim 8. As such, the amount of glycerol taught by Zerbe is inapplicable to the softeners of Becher.

However, even if the amount of glycerol taught by Zerbe was inapplicable to the softeners of Becher (which Applicant disputes), it would still not be obvious to use the claimed amount. In particular, Applicant has already explained how plasticizers were previously employed in an amount of up to 20% by weight based on the amount of polymer, but that phase separations may occur when the percentage amounts of plasticizer

becomes relatively high, so that the films are no longer transparent and their physical properties such as the tear strength are adversely affected. For example, addition of 30% by weight of triethyl citrate, based on the total amount of a crosslinked hydrophilic polymer, leads to white films. The plasticizer may in fact separate out of the film. (See page 2, lines 23-37 of the appellants' specification).

Examiner disregards the above argument as not being directed to the scope of the claims (i.e., glycerol). However, the above argument is clearly related to Examiner's asserted combination. In particular, the disclosed amount of glycerol in the prior art is completely outside the range of Claim 1. Thus, the only way Examiner can assert that there is a reasonable expectation of success of using an increased amount of glycerol is if there is a reasonable expectation of success of using an increased amount of softener/plasticizer in general. However, Applicant has already provided factual evidence that this is **not** the case. As such, Examiner has no reasonable success of using an increased amount of glycerol in combination with a crosslinked hydrophilic polymer above and beyond what has been taught by the prior art. For this reason alone as well, Examiner's asserted combination must fail as providing a case of obviousness.

Furthermore, contrary to Examiner's assertions, the claimed range of 30% to 60% by weight of glycerol as plasticizer, based on the total amount of crosslinked hydrophilic polymers, is most certainly **not** encompassed by the prior art. In particular, as explained above, **none** of the cited art discloses using an amount of glycerol with a polymer film (crosslinked or otherwise) that falls within the claimed range. Rather, the only disclosed amounts of glycerol (i.e., the 20% asserted by Examiner) clearly falls outside the claimed range. It is also pointed out that a reference being silent on how much of an item to include is not the same as saying that any amount is acceptable. In fact, even a specific recitation that any amount can be used is insufficient to actually encompass the claimed range, as such a disclosure is so general and non-specific as to provide no guidance whatsoever to one of ordinary skill in the art as to how much of the item can be used without causing undue experimentation. As such, Examiner's assertions that the claimed range of 30% to 60% by weight of glycerol as plasticizer (based on the total amount of crosslinked hydrophilic polymers) is encompassed by the prior art, is completely without support and thus should be given not weight by the Board.

Moreover, in response to Applicant's statement that it is well known in the art that changing an element in a polymer formulation can drastically affect the properties of the polymer formulation such that there is no expectation of success in making changes to Rupprecht, Examiner splits grammatical hairs and states that only a **reasonable** expectation of success is needed. Applicants have clearly explained how there would be no reasonable expectation of success, citing specific factually examples and common knowledge in the art. Examiner cannot rebut such proof by merely blindly asserting in response that there is a reasonable expectation of success. Splitting hairs over the inclusion of the word "reasonable" ignores to totality of the arguments and evidence provided by Applicant, and provides no further support whatsoever for Examiner's already untenable position.

In fact, the above arguments clearly establish that Examiner lacks a reasonable expectation of success at multiple points in the asserted combination, and that to even arrive at the claimed combination would require undue experimentation. This exponentially magnifies the unreasonableness of the current obviousness rejection.

### *3. Conclusion*

Accordingly, for all of the reasons set forth above, the appellant respectfully asserts that Examiner has failed to establish a *prima facie* case of obviousness of any of the appellant's claims. Therefore, the appellant respectfully requests that the rejection of Claims 1, 6-15, and 18-22 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,780,504 to Rupprecht et al. in view of U.S. Patent No. 6,153,222 to Becher and U.S. Patent No. 6,177,096 to Zerbe et al. be reversed and withdrawn by the Board.

## D. CLAIMS 1, 6-15, AND 18-22 ARE NOT UNPATENTABLE UNDER 35 U.S.C. § 103(A) AS BEING OBVIOUS OVER RUPPRECHT IN VIEW OF BECHER AND U.S. PATENT 6,177,096 TO LYDZINSKI ET AL. ("LYDZINSKI").

On page 6 of the current Office Action, and page 8 of the Examiner's Answer, Examiner rejects Claims 1, 6-15, and 18-22 under 35 U.S.C. § 103(a) as being unpatentable over Rupprecht in view of Becher and Lydzinski. These rejections are respectfully traversed and believed overcome in view of the following discussion.

### *1. Previous Arguments*

The combination of Rupprecht, Becher and Lydzinski is essentially a duplicate rejection of Rupprecht, Becher and Zerbe wherein Lydzinski constitutes a weaker reference than Zerbe. As such, the appellants' arguments presented above against the combination of Rupprecht, Becher and Zerbe are also applicable here and are incorporated by reference.

For the sake of completeness, the appellants note that Lydzinski refers to an oral film containing chemically modified ***starch*** (chemical modification can include crosslinking, but starch is not hydroxypropylmethylcellulose). Potential plasticizers, among others include polyols such as glycerol, but also propylene glycol and sorbitol. Other potential plasticizers include polyesters such as triethyl citrate. (see paragraph [0026] of Lydzinski)

It is not surprising that paragraph [0026] of Lydzinski states that "the plasticizer may be present in any desired amount, particularly from 0 to about 15 percent, more particularly from 0 to about 10 [percent] by weight of the starch component" as these lower ranges are consistent with the state of the art described by the appellants in their specification and repeated in the "Background" section of B.1. above.

Therefore, Lydzinski does not aid in asserting that the combination of Rupprecht, Becher and Lydzinski teaches the appellants' dosage form comprising at least one active ingredient-containing and/or nutrient-containing layer based on in-situ crosslinked hydroxypropylmethylcellulose which comprises from 30% to 60% by weight of glycerol as plasticizer, based on the total amount of crosslinked hydrophilic polymers and whereby the hydroxypropylmethylcellulose has been crosslinked with tannin and/or a crosslinked, optionally partially neutralized polyacrylic acid.

### *2. Reply to Examiner's Answer*

The Examiner's Answer dated March 5, 2012, still seems to overlook, and fails to adequately address, the many of the appellants' arguments above. Further, the Examiner's arguments presented in the Examiner's Answer fail to address the deficiencies of the current rejection.

More specifically, Examiner cites to Rupprecht as relating to a crosslinked hydrophilic polymer and teaching all the requirements of Claim 1 except for the inclusion of glycerol as a plasticizer. As such, Examiner cites to Becher as teaching using a softener

(which can be glycerol) with a crosslinked polymer, and cites to Lydzinski as teaching how much plasticizer to use in a film containing starch (which is not disclosed as contain any crosslinked polymers).

Examiner then asserts that it would be obvious to incorporate the glycol as softener of Becher (used with a crosslinked polymer not disclosed as being hydrophilic) in the amount of plasticizer taught by Lydzinski (which dos not relate to the use of any crosslinked polymers), into the product of Rupprecht (which specifically relates to crosslinked hydrophilic polymers). However, Examiner has established no reasonable expectation of success of such a combination, especially in view of Applicant's prior arguments above.

In particular, Rupprecht actually doesn't teach using any plasticizer at all with a crosslinked **hydrophilic** polymer. As such, the entire combination of Becher (teaching the use of a softener with a crosslinked polymer) with Rupprecht hinges on the assertion that there is a reasonable expectation of success of combining a softener (assumably as a plasticizer) as taught by Becher into the product of Rupprecht.

However, as Applicant has clearly explained above, plasticizers **in general** are not necessarily suitable in the film of Claim 1 (and thus also the combination asserted by Examiner). In particular, Applicant has explained how the use of glycerol in amounts greater than 20% by weight resulted in more desirable products that when polyethylene glycol, sorbitol or triethylcitrate were used as plasticizers and that even when comparing glycerol against itself (20% by weight vs. 50% by weight) a more favorable product was obtained at the higher levels of glycerol content (see Figure 2). As such, success of using plasticizers in general with a crosslinked hydrophilic polymer would **not** be reasonably expected by one of ordinary skill in the art. As such, there can be **no** reasonable expectation of success of including the softener of Becher in the crosslinked hydrophilic polymer product of Rupprecht (which is the only way Examiner arrives at combining glycerol with a crosslinked hydrophilic polymer). For this reason alone, Examiner's asserted combination must fail as providing a case of obviousness.

In addition, Examiner points to Lydzinski as teaching how much plasticizer to use (an example of which is glycerol as per Claim 9 of Lydzinski ). However, it would not be obvious to use the amount glycerol as plasticizer set forth in Claim 1. In particular, Lydzinski does not teach using any amount of plasticizer at all (as Examiner seems to assert), but

rather states that the plasticizer may be present in any **desired** amount, and particularly discloses from 0% to about 15% as such a desired amount, and more particularly from 0% to about 10%. As such, Lydzinski clearly teaches that the upper limit of plasticizer is 15%, with the preferred amount of plasticizer being even less than that. In other words, Lydzinski, nor any of the other cited art, actually discloses, teaches, or suggest using a plasticizer, let alone a glycerol plasticizer, in the amount set forth in Claim 1.

Further, Applicant has already explained how plasticizers were previously employed in an amount of up to 20% by weight based on the amount of polymer, but that phase separations may occur when the percentage amounts of plasticizer becomes relatively high, so that the films are no longer transparent and their physical properties such as the tear strength are adversely affected. For example, addition of 30% by weight of triethyl citrate, based on the total amount of a crosslinked hydrophilic polymer, leads to white films. The plasticizer may in fact separate out of the film. (See page 2, lines 23-37 of the appellants' specification).

Examiner disregards the above argument as not being directed to the scope of the claims (i.e., glycerol). However, the above argument is clearly related to Examiner's asserted combination. In particular, the disclosed amount of plasticizer in the prior art is completely outside the range of Claim 1. Thus, the only way Examiner can assert that there is a reasonable expectation of success of using an increased amount of glycerol is if there is a reasonable expectation of success of using an increased amount of softener/plasticizer in general. However, Applicant has already provided factual evidence that this is **not** the case. As such, Examiner has no reasonable success of using an increased amount of glycerol in combination with a crosslinked hydrophilic polymer above and beyond what has been taught by the prior art. For this reason alone as well, Examiner's asserted combination must fail as providing a case of obviousness.

Furthermore, contrary to Examiner's assertions, the claimed range of 30% to 60% by weight of glycerol as plasticizer, based on the total amount of crosslinked hydrophilic polymers, is most certainly **not** encompassed by the prior art. In particular, as explained above, **none** of the cited art discloses using an amount of glycerol with a polymer film (crosslinked or otherwise) that falls within the claimed range. Rather, the only disclosed amounts of plasticizer (i.e., the 15% maximum asserted by Examiner) clearly falls outside the

claimed range. It is also pointed out that a reference being silent on how much of an item to include is not the same as saying that any amount is acceptable. In fact, even a specific recitation that any amount can be used is insufficient to actually encompass the claimed range, as such a disclosure is so general and non-specific as to provide no guidance whatsoever to one of ordinary skill in the art as to how much of the item can be used without causing undue experimentation. As such, Examiner's assertions that the claimed range of 30% to 60% by weight of glycerol as plasticizer (based on the total amount of crosslinked hydrophilic polymers) is encompassed by the prior art, is completely without support and thus should be given not weight by the Board.

Moreover, in response to Applicant's statement that it is well known in the art that changing an element in a polymer formulation can drastically affect the properties of the polymer formulation such that there is no expectation of success in making changes to Rupprecht, Examiner splits grammatical hairs and states that only a **reasonable** expectation of success is needed. Applicants have clearly explained how there would be no reasonable expectation of success, citing specific factually examples and common knowledge in the art. Examiner cannot rebut such proof by merely blindly asserting in response that there is a reasonable expectation of success. Splitting hairs over the inclusion of the word "reasonable" ignores to totality of the arguments and evidence provided by Applicant, and provides no further support whatsoever for Examiner's already untenable position.

In fact, the above arguments together clearly establish that Examiner lacks a reasonable expectation of success at multiple points in the asserted combination, and that to even arrive at the claimed combination would require undue experimentation. This exponentially magnifies the unreasonableness of the current obviousness rejection.

### *3. Conclusion*

Accordingly, for all of the reasons set forth above, the appellant respectfully asserts that Examiner has failed to establish a *prima facie* case of obviousness of any of the appellant's claims. Therefore, the appellant respectfully requests that the rejection of Claims 1, 6-15, and 18-22 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,780,504 to Rupprecht et al. in view of U.S. Patent No. 6,153,222 to Becher and U.S. Patent Application No. 2003/0099692 to Lydzinski et al. be reversed and withdrawn by the Board.

## IV. CLAIMS APPENDIX

1. (Previously presented)

A dosage form in film form for transmucosal or transdermal administration of at least one active ingredient and/or nutrient to a living creature comprising

at least one active ingredient-containing and/or nutrient-containing layer based on in-situ crosslinked hydrophilic polymers which comprises from 30% to 60% by weight of glycerol as plasticizer, based on the total amount of crosslinked hydrophilic polymers

characterized in that hydroxypropylmethylcellulose is used as hydrophilic polymer and the hydrophilic polymer has been crosslinked with tannin and/or a crosslinked, optionally partially neutralized polyacrylic acid.

2-5. (Cancelled)

6. (Previously presented)

The dosage form as claimed in claim 1, characterized in that the active ingredient-containing and/or nutrient-containing layer comprises at least one active pharmaceutical ingredient or one nutrient.

7. (Original)

The dosage form as claimed in claim 6, characterized in that the active pharmaceutical ingredient is an active ingredient from the group of analgesics, antiallergics, antibiotics, antiemetics, antiseptics, antihistamines, antihypertensives, appetite suppressants, cardiac remedies, chemotherapeutic agents, enzymes, hormones, immunomodulators, inoculations, local anesthetics, psychoactive drugs, spasmolytics, virustatics, vitamins and cytostatics.

8. (Original)

The dosage form as claimed in claim 6, characterized in that the nutrient is a fertilizer.

9. (Previously presented)

The dosage form as claimed in claim 1, characterized in that it has one or more layers.

10. (Original)

The dosage form as claimed in claim 9, characterized in that it has at least one active ingredient-containing and/or nutrient-containing layer, one adhesive layer and/or one covering layer.

11. (Original)

The dosage form as claimed in claim 10, characterized in that at least one active ingredient-containing and/or nutrient-containing layer has a concentration gradient of the active ingredient and/or of the nutrient.

12. (Original)

The dosage form as claimed in claim 10, characterized in that the covering layer is impermeable for the active ingredient.

13. (Previously presented)

The dosage form as claimed in claim 1, characterized in that it is covered by a protective layer before application.

14. (Previously presented)

The dosage form as claimed in claim 1, characterized in that the living creature is a human or an animal.

15. (Previously presented)

The dosage form as claimed in claim 1, characterized in that the transmucosal or transdermal administration is buccal administration.

16-17 (Cancelled)

18. (Previously presented)

The dosage form as claimed in claim 1, characterized in that it has at least one active ingredient-containing and/or nutrient-containing layer, one adhesive layer and/or one covering layer.

19. (Previously presented)

The dosage form as claimed in claim 18, characterized in that at least one active ingredient-containing and/or nutrient-containing layer has a concentration gradient of the active ingredient and/or of the nutrient.

20. (Previously presented)

The dosage form as claimed in claim 19, characterized in that the covering layer is impermeable for the active ingredient.

21. (Previously presented)

The dosage form as claim in claim 20, characterized in that the ratio of hydrophilic polymer to crosslinker is from 2:1 to 5:1 by weight.

22. (Previously presented)

The dosage form as claimed in claim 21, characterized in that the at least one active ingredient and/or nutrient is prednisolone.

## V. EVIDENCE APPENDIX

None.

## VI. CONCLUSION

In view of the foregoing, it is submitted that the rejections of the Examiner based on the art of record is improper. Accordingly, it is requested that this Board reverse the Rejection Raised by the Examiner.

Respectfully submitted,

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